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RADIUM

A MONTHLY JOURNAL DEVOTED TO THE CHEMISTRY, PHYSICS AND THERAPEUTICS OF RADIUM AND OTHER RADIO-ACTIVE SUBSTANCES

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VOL. II MARCH, 1914 NO. 6

CONTENTS

	Page
The Intravenous Injection of Soluble Radium Salts, III, by Frederick Proescher, M. D.	77
Notes and Comments	87
Reviews and Abstracts	91

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RADIUM

A MONTHLY JOURNAL DEVOTED TO THE CHEMISTRY, PHYSICS AND THERAPEUTICS OF RADIUM AND OTHER RADIO-ACTIVE SUBSTANCES

PUBLISHED BY THE RADIUM PUBLISHING COMPANY
FORBES AND MEYRAN AVENUES, PITTSBURGH, PA.

We shall be glad to receive for publication from our subscribers and readers articles pertaining to the subject of radium and its application. All inquiries for information will be accorded prompt attention, and will be answered either by letter or through the columns of this paper.

VOL. II MARCH, 1914 No. 6

THE INTRAVENOUS INJECTION OF SOLUBLE RADIUM SALTS. III.

By FREDERICK PROESCHER, M. D.

Director of the Laboratory for Experimental Therapy, Standard Chemical Company.

In the following are presented the results of the intravenous injection of soluble radium salts upon the blood pressure in the polyarthritis cases.*

The blood pressure was estimated with a Faught aneroid sphygmomanometer by the palpation method, and by the asculatory method with the sphygmometroscope (Prendergast). The term systolic blood pressure (maximal pressure) means the degree of arterial pressure in the arterial system during the cardiac systole; diastolic blood pressure (minimum pressure) the degree of arterial pressure existing in the arterial system preceding the systole. The difference between the systolic and diastolic pressure represents the pulse pressure, indicating the amount of periodic variation in blood pressure within the arterial system as the result the intermittent action of the heart. The average maximum blood pressure for males at all ages is 127.5 mm., for females 120 mm. All determinations were made with the patient sitting in a reclining posture.

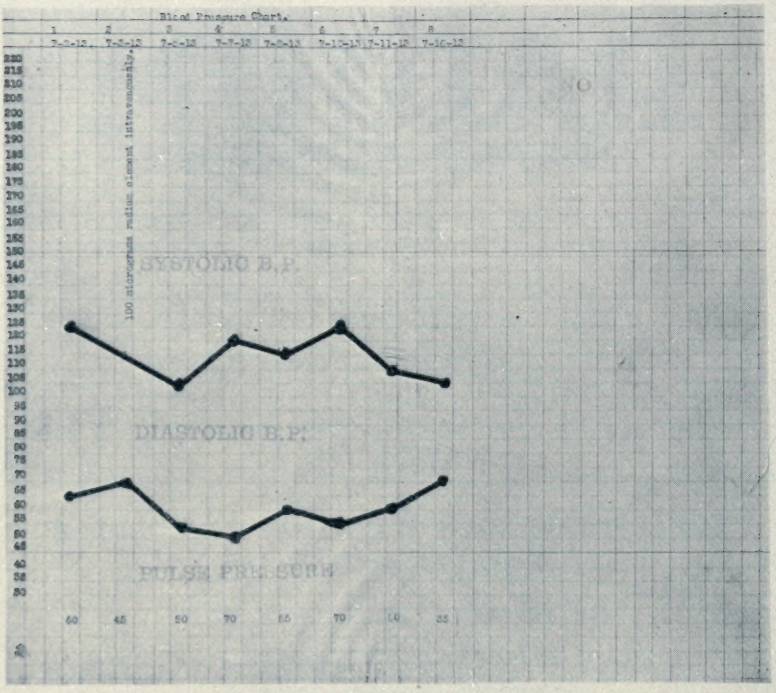
CASE No. 2†.

BLOOD PRESSURE.

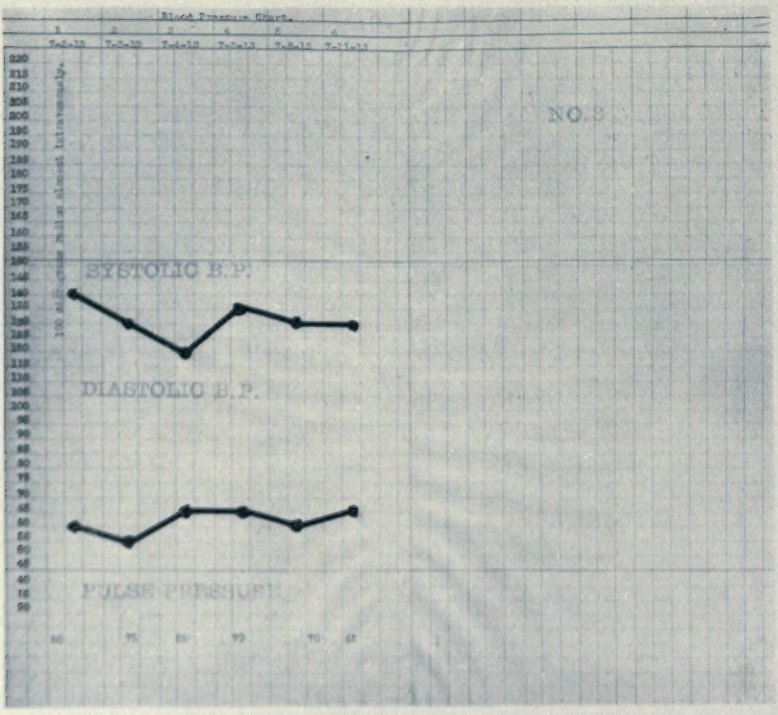
Date	Systolic	Diastolic	Pulse Pressure
7- 2-13	125	65	60
7- 3-13	115	70	45
	100 micrograms radium element intravenously.		
7- 5-13	105	55	50
7- 7-13	120	50	70
7- 8-13	115	60	55
7-10-13	125	55	70
7-11-13	110	60	50
7-16-13	105	70	35

*See preceding articles by Dr. Proescher, in January and February numbers of RADIUM, in which reports were given on sixteen cases of arthritis treated by the intravenous injection of soluble radium salts.

†In case No. 1 and case No. 16 no blood pressure was taken.



Case No. 2.



Case No. 3.

CASE No. 3.

BLOOD PRESSURE.

Date	Systolic	Diastolic	Pulse Pressure
7- 2-13	140	60	80
	100 micrograms radium element intravenously.		
7- 3-13	130	55	75
7- 4-13	120	65	55
7- 5-13	135	65	70
7- 8-13	130	60	70
7-11-13	130	65	65

CASE No. 4.

BLOOD PRESSURE.

Date	Systolic	Diastolic	Pulse Pressure
7- 3-13	120	75	45
	100 micrograms radium element intravenously.		
7- 4-13	115	70	45
7- 9-13	110	65	45
7-10-13	105	65	40
	100 micrograms radium element intravenously.		
7-11-13	105	65	40
7-12-13	100	55	45

CASE No. 5.

BLOOD PRESSURE.

Date	Systolic	Diastolic	Pulse Pressure
7- 6-13	125	90	35
	100 micrograms radium element intravenously.		
7- 8-13	105	70	35
7- 9-13	105	75	30
7-13-13	105	75	30

CASE No. 6.

BLOOD PRESSURE.

Date	Systolic	Diastolic	Pulse Pressure
7- 3-13	110	70	40
	100 micrograms radium element intravenously.		
7- 4-13	130	80	50
7- 5-13	115	70	45
7- 7-13	120	80	40
7- 8-13	105	65	40
7- 9-13	115	65	50
7-10-13	105	65	40
7-11-13	115	75	40
7-12-13	110	85	25
7-14-13	110	85	25

CASE No. 7.

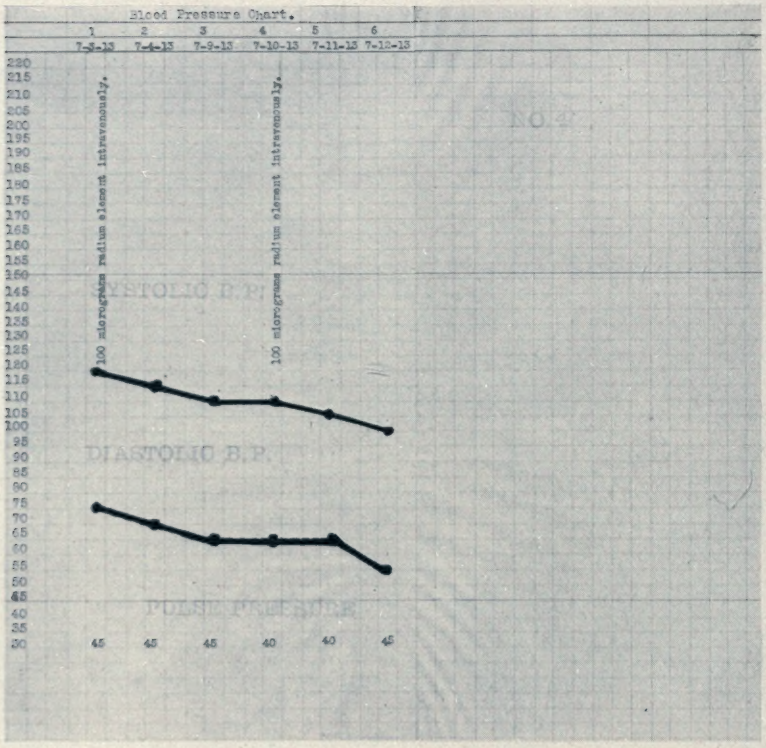
BLOOD PRESSURE.

Date	Systolic	Diastolic	Pulse Pressure
7- 8-13	105	80	25
	100 micrograms radium element intravenously.		
7- 9-13	110	70	40
7-19-13	110	75	35
7-20-13	105	75	30
7-24-13	105	75	30

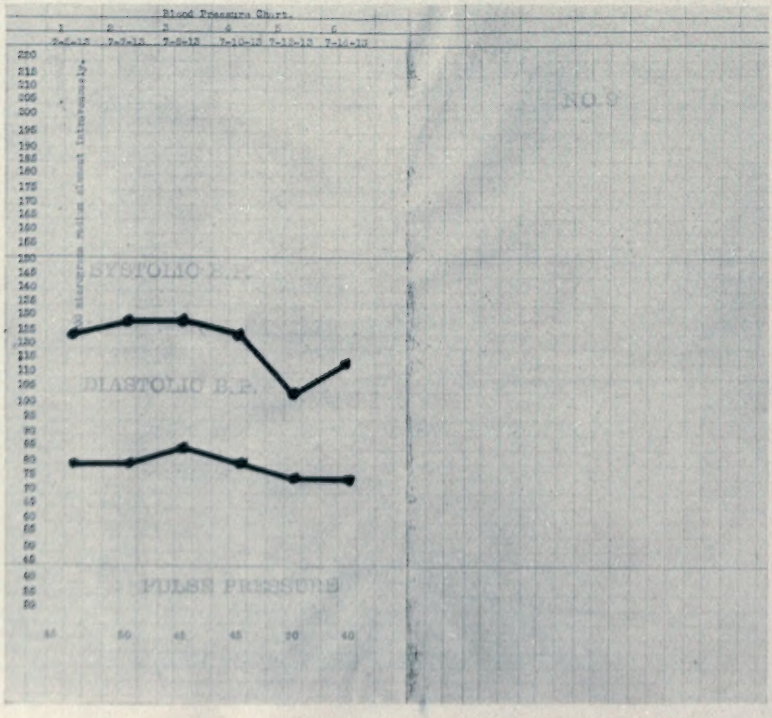
CASE No. 8.

BLOOD PRESSURE.

Date	Systolic	Diastolic	Pulse Pressure
7-19-13	155	60	95
	100 micrograms radium element intravenously.		
7-21-13	125	65	60
7-23-13	135	60	75



Case No. 4.



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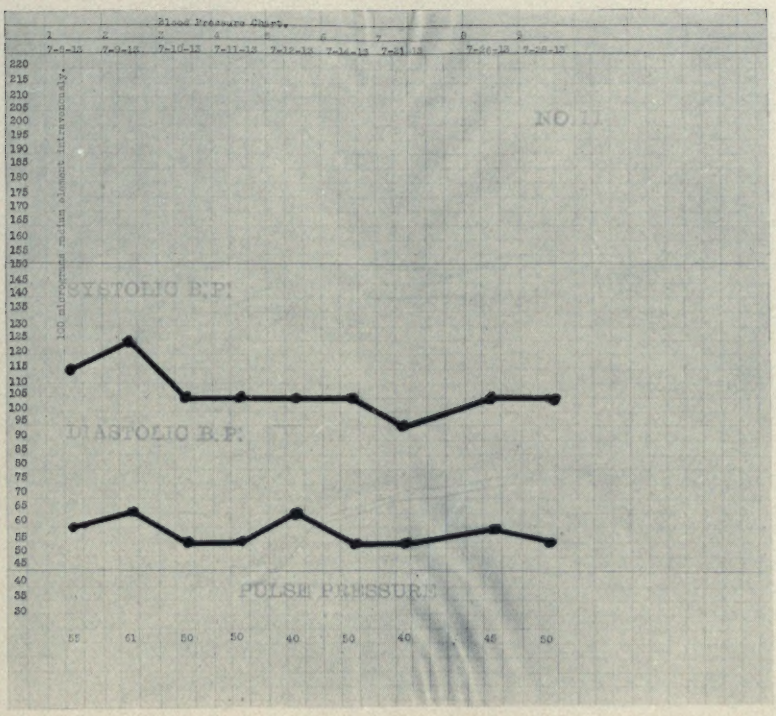


Case No. 11

CASE No. 9.

BLOOD PRESSURE.

Date	Systolic	Diastolic	Pulse Pressure
7- 5-13	125	80	45
	100 micrograms radium element intravenously.		
7- 7-13	130	80	50
7- 8-13	130	85	45
7-10-13	125	80	45
7-12-13	105	75	30
7-14-13	115	75	40

CASE No. 10.

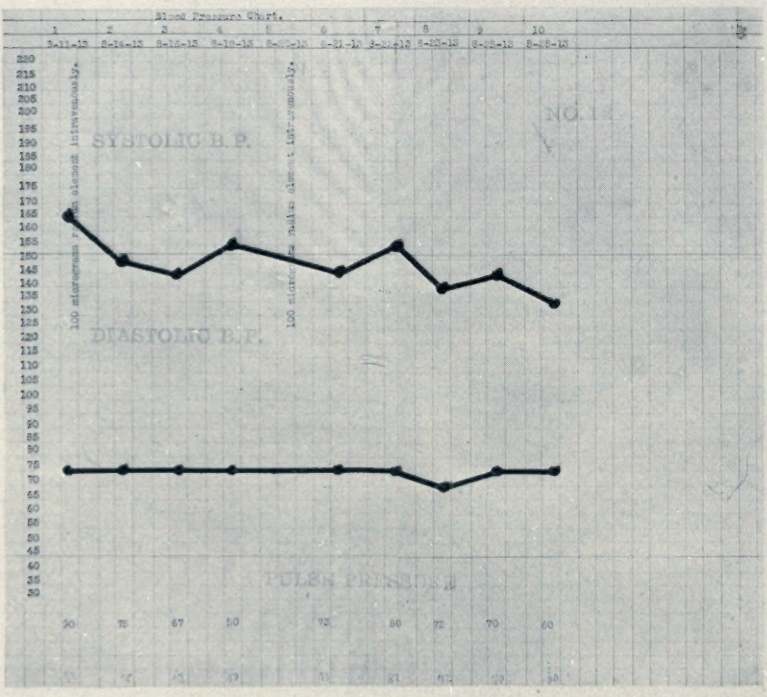
BLOOD PRESSURE.

Date	Systolic	Diastolic	Pulse Pressure
7-14-13	110	75	35
	100 micrograms radium element intravenously.		
7-21-13	115	75	40

CASE No. 11.

BLOOD PRESSURE.

Date	Systolic	Diastolic	Pulse Pressure
7- 8-13	115	60	55
	100 micrograms radium element intravenously.		
7- 9-13	126	65	61
7-10-13	105	55	50
7-11-13	105	55	50
7-12-13	105	65	40
7-14-13	105	55	50
7-21-13	95	55	40
7-26-13	105	60	45
7-28-13	105	55	50



Case No. 12

CASE No. 12.

BLOOD PRESSURE.

Date	Systolic	Diastolic	Pulse Pressure
8-11-13	165	75	90
	100 micrograms radium element intravenously.		
8-14-14	152	77	75
8-16-13	145	77	67
8-18-13	155	75	80
	100 micrograms radium element intravenously.		
8-21-13	145	72	73
8-22-13	155	75	80
8-23-13	142	70	72
8-25-13	147	77	70
8-28-13	135	75	60

CASE No. 13.

BLOOD PRESSURE.

Date	Systolic	Diastolic	Pulse Pressure
8-13-13	102	50	52
	100 micrograms radium element intravenously.		
8-15-13	97	65	32
8-18-13	97	62	35

CASE No. 14.

BLOOD PRESSURE.

Date	Systolic	Diastolic	Pulse Pressure
8-11-13	127	77	50
	100 micrograms radium element intravenously.		
8-14-13	117	72	45
8-16-13	132	77	55
8-18-13	130	77	55

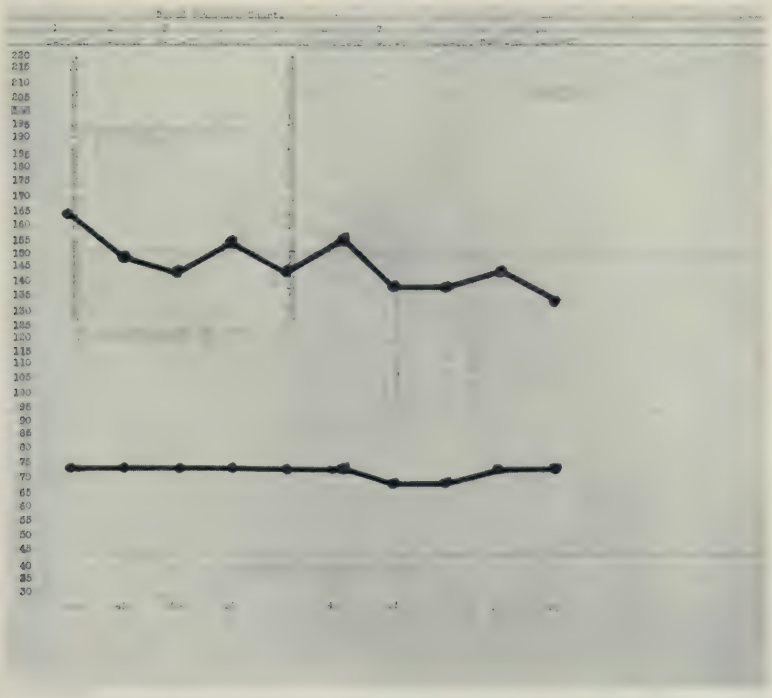
	100 micrograms radium element intravenously.		
8-21-13	120	75	45
8-22-13	125	70	55
8-23-13	112	70	46
8-25-13	120	85	35
8-26-13	125	75	46

CASE No. 15.
BLOOD PRESSURE.

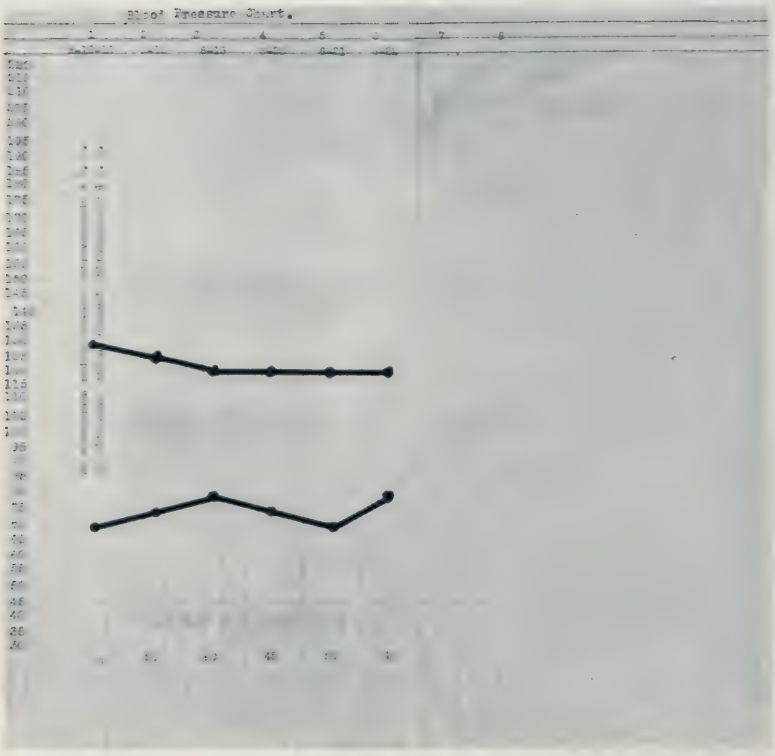
Date	Systolic	Diastolic	Pulse Pressure
8-15-13	130	70	60
	50 micrograms radium element intravenously 1:00 P. M.		
	50 micrograms radium element intravenously 4:00 P. M.		
8-16-13	125	75	50
8-18-13	120	80	40
8-20-13	120	75	45
8-21-13	120	70	50
8-22-13	120	80	40

In twelve cases (80% of all the cases) the blood pressure was reduced on an average of about 20 mm. in from one to eight days. In two cases (13⅓% of all the cases) no reduction was noticed. The effect of the radium on the circulatory system will be discussed in a later paper.

CONCLUSIONS. It is rather early from the relatively few cases of polyarthritis treated to draw any definite conclusions as to the therapeutic value of the intravenous application of radium. Considering the more or less chronic course of the polyarthritis with its periods of



Case No. 14



Case No. 15.

aggravation and at other times improvement without any medication, makes it very difficult to establish the true value of a new therapy. The clinical observation can very easily lead to a deception, if one is not thoroughly acquainted with the course of the disease process. To exclude errors it is necessary to keep the patient under constant observation, and make repeated examinations over longer periods, after medication is stopped. The foregoing reported therapeutic results with the intravenous radium therapy are only preliminary, because the time of observation is too short to make a definite statement as to the permanence and protection against recurrence.

I have used the terms "temporarily cured", "considerably improved", and "improved" to classify achieved results. Temporarily cured cases are those which are entirely free from all subjectve and objective symptoms and have no limitation in the movement of the joints. Such results can only be obtained in such cases in which the morbid process exists only for a short time and no degenerative changes have taken place. In the more advanced cases with objective changes in the joints, I used the terms "much improved" and "improved" because these cases show only an improvement consisting in a decrease or disappearance of pain and retrogression of the inflammatory swelling, as degenerative changes in the cartilage cannot be influenced. We are at present not informed as to the etiological agent causing the polyarthritis, we therefore do not know whether the radium has any direct specific effect upon the unknown cause or whether it has only a symptomatic one, acting as an analgetic and antiphlogistic agent upon the diseased joints. Without doubt radium has a specific selective effect

upon rheumatic diseased joints which is shown by the increased pain and inflammatory reaction after a radium injection. I presume that under the influence of the rheumatic cause a chemical change in the diseased cartilage takes place, probably in splitting of chondritin-sulphuric acid, which on account of the sulphuric acid radical has an increased affinity for the radium.

The soluble radium salt is probably deposited as an insoluble sulfate in the diseased joints. The theoretical hypothesis could be experimentally proved by estimation of the radium content found in the diseased cartilage.

Reaction, namely pain and stiffness, in the joints was noticed in fifteen cases. In eight cases inflammatory swelling was observed which subsided in from two to twenty-two days after the injection. In three cases the patients claimed that they had slept unusually well, and in ten cases the marked general improvement was claimed by the patients between two and twenty-two days after the injection. No alarming symptoms were observed in any of the cases. The temperature and pulse did not show any considerable change. In a few cases the patients noticed an increase in the urine secretion.

In the following tables we compare the results of the radium emanation therapy as obtained by *Gudzent* in 247 cases of polyarthritis, with the intravenous radium therapy:

Radium Emanation Therapy.			Radium Injection Therapy.		
Considerably improved	62	25%	Temporarily cured	4	25%
Improved	81	33%	Considerably improved	8	50%
Slight improvement	52	21%	Improved	2	12.5%
No improvement	52	21%	No improvement	2	12.5%

It will be noted that the intravenous radium injection has a more marked therapeutic effect than radium emanation therapy. The most favorable cases for radium treatment are the acute and subacute and the not too far advanced cases of chronic polyarthritis. Very little or no effect was noted in the arthritis deformans except in one case which showed a fairly good improvement. As to whether intravenous radium therapy in acute cases with high fever is indicated, is an open question. In one case of acute polyarthritis which I have treated recently I gave 50 micrograms during a temperature of 102° without injurious effect. About 24 hours after the injection the pain in the joints entirely subsided. Further experience with a larger number of acute cases is necessary in order to prove whether radium is indicated in all acute cases.

According to our experience 100 to 200 micrograms of radium element should be a sufficient dose in the treatment of polyarthritis. It seems to be advisable to give radium in fractional doses, for instance 100 micrograms in four doses of 25 micrograms, or two doses of 50 micrograms each, given every other day or 200 micrograms in 50 microgram doses given every other day.

In cases of recurrence radium injection can be repeated without any fear of danger as to the accumulative effect of the radium. According to our latest animal experiments the lethal dose for a human being would be about 60 milligrams.

THE INFLUENCE OF RADIUM ON THE BLOOD. In twelve cases (80% of all the cases) an increase of from 250,000 to 1,175,000 in the red cells was noticed. It is striking to note that the case injected with only 40 micrograms showed the highest increase of the red cells. Two cases (13⅓% of all the cases) showed a decrease of the red cells, one 450,000 and one 750,000. The haemoglobin was increased in 11 cases, (73⅓% of all the cases), and in four cases (26⅔ % of all the cases) no increase was

observed. The haemoglobin showed a marked decrease in eight cases, (3, 4, 5, 6, 7, 9, 12, 14) twenty-four hours to a few days after the injection with a subsequent return to normal or an increase in haemoglobin. The number of red cells in spite of the low haemoglobin content was not altered very much. Whether this quantitative change in the haemoglobin content is due to a chemical alteration of the haemoglobin by action of radium which changes the color so that exact determinations cannot be made with the haemoglobinometer or to an output of premature red cells with less haemoglobin, has not yet been determined.

The microscopic examination of the stained blood films of these cases did not show any morphological changes in the red cell (polychromasie macro or microcytosis or punctated red cells). No neucleated red cells were found. It would appear from this that the low haemoglobin content which was observed in half of the cases after the injection of radium is more likely due to a change in the color and not to a rapid destruction of the red cells, as we should find in the latter, premature red cells. Whether the numerical increase in the red cells in the circulating blood stream is due to an increased production of the red cells or a temporary chemotactic effect which introduces into the blood stream the reserve fund of the mature red cells I leave open for further investigation. The increase of the red cells is only temporary as they slowly return to normal.

The leucocytes were slightly reduced in ten cases, the lowest count observed being 4000. In five cases there was no decrease but a slight leucocytosis. The variations in the differential count are not very pronounced, the neutrophiles are more or less slightly increased. The same is observed in the eosinophiles, which show very little variation from the normal, save in one case where an increase of nearly 6% was noted.

The lymphocytes show more or less slight decrease followed in some cases by a slight increase. The monocytes and also the basophiles show a tendency to a slight increase. No morphological changes in the leucocytes in the stained films were observed.

I herewith give the following results obtained after intravenous injection of radium in sixteen cases of polyarthritis:–

Temporarily cured	4	25%
Considerably improved . . .	8	50%
Improved	2	12.5%
Unimproved	2	12.5%

TABLE SHOWING THERAPEUTICAL RESULTS OBTAINED.

Temporarily Cured Cases.

Acute polyarthritis, 18 days duration.
Chronic progressive polyarthritis, four years duration.
Subacute polyarthritis, three months duration.
Chronic polyarthritis, two and one half years duration.

Considerably Improved Cases.

Chronic polyarthritis 1, four months duration.
Chronic progressive polyarthritis 7, two months to forty years duration.

Improved Cases.

Chronic progressive polyarthritis 1, six months duration.
Chronic progressive polyarthritis 1, one year duration.

Unimproved Cases.

Oligoarthritis deformans 2, from four to nineteen years duration.

TABLE SHOWING THE AMOUNT OF RADIUM INJECTED IN THE ARTHRITIS CASES.

CASES	Amt. radium injected	Total amt. radium
No. 1 Acute polyarthritis	10, 20, 20 micrograms	40 micrograms
No. 2 Chronic progressive polyarthritis .	100 "	100 "
No. 3 Chronic polyarthritis . . .	100, 50 "	150 "
No. 4 Subacute polyarthritis . . .	100, 100 "	200 "
No. 5 Chronic progressive polyarthritis .	100, 50 "	150 "
No. 6 Chronic progressive polyarthritis .	100, 50, 50 "	200 "
No. 7 Oligoarthritis deformans . . .	100, 250 "	350 "
No. 8 Oligoarthritis deformans . . .	100, 30 "	130 "
No. 9 Chronic progressive polyarthritis	100 "	100 "
No. 10 Chronic progressive polyarthritis	100, 50 "	150 "
No. 11 Chronic progressive polyarthritis	100, 50 "	150 "
No. 12 Chronic progressive polyarthritis	50, 100 "	150 "
No. 13 Oligoarthritis deformans . . .	100 "	100 "
No. 14 Chronic progressive polyarthritis	50, 50 "	100 "
No. 15 Chronic progressive polyarthritis	50, 50 "	100 "
No. 16 Chronic polyarthritis . . .	100 "	100 "

TABLE SHOWING THE AMOUNT OF RADIUM INJECTED AND EFFECTS ON THE BLOOD PRESSURE.

	Amount of radium injected	Systolic pressure before injection	Systolic pressure after injection	Reduction
Case No. 2	100 micrograms	123 mm.	105 after 1 day	20 mm.
3	100 "	140 "	120 " 2 "	20 "
4	200 "	120 "	100 " 3 "	20 "
5	100 "	125 "	105 " 4 "	20 "
6	100 "	110 "	105 " 3 "	20 "
7	100 "	No reduction.		
8	100 "	155 mm.	125 " 1 "	30 "
9	100 "	125 "	125 " 4 "	20 "
10	100 "	No reduction.	105	
11	100 "	115 mm.	95 " 6 "	20 "
12	200 "	165 "	135 " 8 "	30 "
13	100 "	102 "	97 " 1 "	5 "
14	200 "	127 "	112 " 6 "	15 "
15	100 "	130 "	120 " 3 "	10 "

NOTES AND COMMENTS

One of the most interesting sessions of the Clinical Congress of Surgeons of North America was the symposium upon radio-active treatment of various kinds, the subject that was discussed Wednesday and Thursday nights. Among those taking part were Profs. Bernhard *Kroenig* and C. J. *Gauss*, of the University of Freiburg, Germany and Prof. Howard A. *Kelly*, of Baltimore. The German physicians demonstrated their technic of radiotherapy in the treatment of cancer at Wesley Hospital.

In the discussion on this subject, Doctor *Kelly* told of the treatment of forty cases of cancer. He declared that two cases of carcinoma of the breast seemed to have been cured by the use of radium. This substance also is sometimes curative, he declared, in cancer of the nose, eyes, and lips; and it will produce good cosmetic results where surgical measures would mutilate and disfigure. Doctor *Gauss* said that the

X-ray, radium, and mesothorium had all been used in Freiburg with excellent results, both temporary and permanent.

Dr. Thomas S. *Cullen*, of Baltimore, sounded a word of warning, saying that nothing is more to be feared than the use of radium in nostrums of any kind. "Radium should be standardized, so that the buyer knows what he is paying for," he continued: "and only time will tell what percentage of cases can be cured with radium." At present early surgical operation affords the best chance for cure. However, the results obtained from radium must be taken into consideration.

* * * * *

Consul Milo A. *Jewett*, of Kehl, in the Daily Consular and Trade Reports for January 29th, 1914, notes that the Strassburg (Germany) Hospital and University some time ago bought 200 milligrams of radium (bromide) at $76 per milligram, and has bought 100 milligrams more, which will cost at present prices $98 per milligram. This is at the rate of about $183 per milligram of radium element contained in the radium bromide.

* * * * *

T. *Nogier*, reports on the Biological Action of Radium, in the "Lyon Medical", December 7, 1913. He exposed the seeds of four different plant species to various concentrations of radium emanation, and observed the subsequent effects on growth when they were planted. The larger doses caused a complete loss of sprouting power, though the different seeds showed variations in the amount required, small seeds proving more resistant than the larger. A dose just insufficient to sterilize the seed resulted in a stunted growth, soon followed by signs of senescence and death of the plant. Intermediate doses caused slow and incomplete growth, with delay in blooming. Small doses caused initially retarded, scanty growth followed in two months by growth so rapid that the plants eventually became larger than the untreated controls, though flowering was somewhat delayed. These last observations demonstrate the excitant effect of small doses of radium, and probably, by analogy, may be said to imply danger in the clinical use of radium where the amount available is insufficient and the exposures too brief.

* * * * *

The Chemiker Zeitung for January 16th, 1914 (p. 70) says of radium that the commonest radium salts when pure (100%) have the following radium (element) content: radium bromide ($Ra\ Br_2\ 2H_2O$) 53.6%, radium sulfate ($Ra\ SO_4$) 70.2%, radium chloride ($Ra\ Cl_2$) 76.1%, radium carbonate ($Ra\ CO_3$) 79.0%, and as sold these salts are usually from 50% to 60% pure. In the sale of such radium salts, the price is always based upon the radium element content or the content of pure (100%) radium salt.

* * * * *

Charles H. *Viol*, Ph. D. and William H. *Cameron*, M. D. of Pittsburgh, Pa., addressed the Philadelphia Clinical Association, February 2nd, on the subject of "Radium". Dr. *Viol* told of the physical properties of radium, its decay products and the rays, and demonstrated these, 270 milligrams of radium element in the form of various salts being shown. Dr. *Cameron* spoke of his experiences in the internal use of radium and the local application of radium in cancer.

* * * * *

An anonymous donor has presented the University of Buda Pest with $30,000 for the purchase of two hundred milligrams of pure radium bromide.

The Harvard Alumni Bulletin for January 28th, 1914 contains an article on the Harvard Investigation of Radium, from which we give the following extracts:–

"The Cancer Commission of Harvard University, working in conjunction with the Harvard Medical School, has been experimenting for some time with radium and its derivatives as a cure for, or alleviation of, cancer, and from these experiments, a number of valuable observations have already been recorded. The Harvard authorities at present take a conservative view of the value of radium, but able men are on the commission, and they plan to pursue their investigations indefinitely, with the hope of determining eventually just what radium and its derivatives can do."

"Harvard is the first college in the country to take up this study in this thorough way; for the experimentation is being conducted in its laboratories and a considerable number of patients are being treated by radium at the Collis P. Huntington Memorial hospital, where careful records, illustrated by photographs, tracings and measurements are kept, that the benefit of radium therapy may be determined. Correlation of the clinical and pathological data and careful observation of all cases for final results of treatment are necessary for accurate clinical work."

"In each case, which comes under observation, exact microscopic evidence is obtained, for it is important to know with certainty whether a true cancer, or something which superficially resembles a cancer, is the subject for treatment."

"The commission has the resources of Harvard University behind it in this work, and that ability and experience are not lacking is apparent in the personnel of the commission, of which the members are as follows:—Dr. J. Collins *Warren*, chairman; Dr. Henry P. *Walcott*, of the Harvard Corporation; Dr. Edward H. *Bradford*, dean of the Harvard Medical School; Dr. Theobald *Smith*, professor of comparative pathology and Dr. William T. *Councilman*, professor of pathology, Harvard Medical School; Dr. Henry K. *Oliver*, trustee of the Caroline Brewer Croft Fund; Dr. Robert B. *Greenough*, secretary and consulting surgeon; Dr. Henry A. *Christian*, consulting physician; Arthur *Adams*, treasurer; Dr. E. E. *Tyzzer*, director; Dr. Thomas *Ordway*, physician in charge of the Huntington Hospital, and Dr. William *Duane*, Physicist."

"Dr. *Duane* was for six years an assistant in the Curie Laboratory in Paris, and is one of the foremost men in radium experimentation in this country. Dr. *Ordway* has recently investigated the status and methods of radium therapy in London and on the continent. Dr. *Tyzzer* supervises the biological and pathological work in which radium is used."

The Harvard Cancer Commission makes the following statement:— "In certain limited cases, treatment by radium seems to be curative, while in others, not cured by this agent, local results are good and such distressing symptoms as pain, hemorrhage and discharge may be greatly benefitted. At the present time, however, the most satisfactory treatment of cancer is generally admitted to be the complete removal by surgical operation at the earliest possible moment. The best, or curative results from radium therapy, are obtained in cases of various skin diseases, including certain types of skin and other localized forms of cancer."

"In many cases of true cancer which have advanced beyond the operable stage, or cases recurring following operation, improvement after radium treatment may follow not only symptomatically, but in the local condition. Such cases, however, are rarely cured. Occasionally large growths are much reduced and even disappear under the influence of radium, but matastasis, or spreading of the growth to other parts, is not usually prevented, or the patient may succumb from toxemia during the process of absorption."

"Great variations occur in different types of cancer in the same and in different individuals. In some cases the entire duration of the disease is short-months; in others it may last for years, as many as twelve or fifteen, and there may be periods of great temporary improvement. But the fact cannot be too strongly emphasized that this variability in the natural history of new growths may account for many of the favorable results supposedly due to therapeutic procedures."

"Owing to the possible exaggeration and misinterpretation of the result of radium therapy, it is deemed most important that ample and accurate clinical data be secured and the results recorded in a form suitable for critical analysis. It is to obtain such accurate observation of the effect of radium treatment, to devise new and more effective methods of administration and to give to the public the unprejudiced result of these investigations that the Cancer Commission of Harvard University is devoting its energies."

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In the January 31st, 1914 number of the Scientific American Supplement, Prof. C. F. *Brown* gives evidence from geological data to show that the element sodium is undergoing radio-active disintegration.

"By the usual test for radio-activity, i. e., the continued ionization of a gas independent of other physical conditions, sodium as an element does not display any activity that is definitely greater than that found in all matter. And the ionizing activity of ordinary matter is so slight that it cannot be stated with definiteness whether or not the matter is of itself radio-active. But radio-activity implies a more fundamental change than that of emitting matter and energy continuously. It implies an atomic disintegration. If alpha particles are emitted the atoms go by leaps and bounds to new atoms of other properties, while if beta and gamma radiations are emitted the wearing away of the atoms must be just as certain, though no one has been able to conjecture by what steps the changes may take place."

"The fact that a given element does not give out a measurable ionizing radiation is not necessarily evidence that it is not radio-active."

"If sodium is a radio-active element we may at present look for other evidence than direct radiations. We shall inquire whether in past geologic time sodium has accumulated radio-actively from other matter or on the other hand whether sodium has disappeared or disintegrated into other forms of matter."

"The best evidence that we have for considering sodium a radio-active element is from geology. If the age of the earth is determined from radio-active data, and the value accepted, we find that there is not accumulated in the ocean basin as much sodium as there would have accumulated during this time."

The present estimated annual outputs from rivers of chlorine and of sodium (in metric tons x 1000) are 155,350 and 158,357 respectively, whereas the amounts of chlorine and sodium in the ocean (in metric

tons multiplied by one million million) are 25,538 and 14,138 respectively."

"The geologists do not believe that the rivers carried on the average any less sodium previously than they do now. But if they did, they should have also carried less chlorine. We may, therefore, for checking purposes say that nothing concerning the annual river output further than it should have varied alike with sodium and chlorine. On this assumption the above figures show that there is not as much sodium in the ocean as there should be. We see that the above evidence favors the radio-active decay of sodium as an element."

REVIEWS AND ABSTRACTS.

Isaac *Levin*. Radium and Roentgen Therapy in Cancer. Medical Record. Vol. 84, pp. 1064-68, (1913). A paper read at the meeting of the Section of Medicine of the New York Academy of Medicine, October 21st, 1913. *Levin* compares the action of the X-rays and the radium rays upon cells to that of the salvarsan used in syphilis. The latter substance kills the spirochetae pallidae without injuring the normal tissues of the organism of the host and in the case of the rays there is a selective action on the cancer cells. The advance in technique in the past several years has been remarkable.

"In order to place a true valuation on the radiotherapy in cancer a comparison with salvarsan may be again in place. A true radical cure of cancer with every cell destroyed is as rare as the therapia magna sterilisans in salvarsan therapy. One must not forget that the initial lesion in syphilis during the first few days does not penetrate any deeper than an epithelioma of the skin, and the latter can be radically cured by radiotherapy. But in the deeper conditions by no means every case responds as promptly and as well. I have seen cases of carcinoma of the uterus where the action of the radium was marvelous, and I have seen again cases which seemed to be identical clinically and microscopically, and still do not respond to the action of radium."

"I have also seen cases where the patient after treatment with radium appeared to be clinically well and the microscope showed only a few islands of carcinoma cells remaining. The treatment was discontinued for a couple of weeks, and the patient returned with a local recurrence of the carcinoma."

"Radiation undoubtedly accomplishes as much as the knife in certain localized superficial conditions like the epitheliomata of the skin and ulcus rodens. It may even have certain advantages over the operative treatment inasmuch as it may reach microscopically small islands of cancer cells which the knife would have left behind. Furthermore, it does not open the lymph and blood channels and allow freed cancer cells to enter the circulation as an operative incision may do. On the other hand, the size and extent of the tumor growth may be such as to preclude the possibility of its being influenced in its entirety by the rays. Should the main mass of the tumor be removed surgically then the rest can be easily influenced by the rays."

"Figs. 4 and 5 *present schematic drawings of a carcinoma of the breast and one of the uterus. One radium tube is shown over the skin of the breast, and this tube will not be able to influence the whole of the tumor. Another radium tube is shown on the wall of the chest after the tumor has been removed surgically. This tube will have to influence the remaining islands of carcinoma, which is surely easier of accomplishment. The rays may also be brought in better contact

*Not reproduced here.

with all the parts of the tumor by inserting the tube in the center of the growth, but a preliminary radical removal of the tumor is certainly a better procedure. In the case of a cancer of the uterus the tube can be placed in nearer contact with all the parts of the tumor, as is seen on the illustration, and in a certain number of cases all the cancer cells within the uterus may be destroyed. But even in this case a few islands of cancer cells may remain and give rise subsequently to recurrence."

"In view of all of these considerations the advisability of radiation as an only method of treatment of inoperable cases of cancer appears to me to be very questionable. In the present state of our knowledge I must emphasize strongly that the radical operative removal remains the paramount method of treatment in cancer whenever practicable."

"But in certain cases it may be advisable to radiate before the operation. The cases reported that were made operable through a preliminary radiation indicate the advantage of such a mode of procedure. Certain cases have also been reported where the radiation did not diminish the size of the malignant growth and still the condition seemed to have become more benign and the life of the patient was prolonged from a few months to a few years. A preliminary radiation may then improve the ultimate results of the operation. The same reasoning indicates clearly the absolute necessity of prophylactic radiation following every operation for a malignant growth. Inoperable cases belong indisputably to the domain of radiotherapy. But here another extreme must be guarded against. Cases with metastases in the liver and lungs and general dissemination should not be turned over as an ultimum refugium for radium therapy. This will serve only to discredit the method of treatment and demoralize scientific work. Barely 20% of the cases referred to me for radium treatment are suitable. The attending physician or surgeon should begin to consider radium early in his treatment of cancer cases, and not when the patient is moribund."

"The radio-active substances are the most powerful chemical agents of any that we know at present, and a wildly proliferating cancer cell is the most treacherous enemy to handle. Too small a dose of radium may irritate and increase the growth of cancer, instead of arresting it. Too large a dose may necrotize the cancer tissue too rapidly and produce perforations into vital organs (esophagus, stomach, colon, etc.), or erode the blood vessels and produce a fatal hemorrhage. Very large doses may produce, also, alarming general symptoms–fever, nausea, and even collapse. Correct and scientific methods of radium and Roentgen therapy, methods which will lead to real progress in the future treatment of malignant growths, imply the correct selection of cases, correct dosage and filtration of the rays, and constant clinical and microscopical control of the patient under treatment. In other words, the physician who takes up radiotherapy as his life work and wants to protect himself and his patients against great disappointments and serious mishaps should not only be well acquainted with the physical and biological properties of the rays, but must also be a trained clinical surgeon and a pathologist."

"To recapitulate:—The radium and Roentgen rays are no more of a cancer cure than salvarsan is a syphilis cure, but these rays are therapeutic agents deserving at least as much consideration as surgery. Over-enthusiasm is as injurious to scientific work as over-pessimism is. Sober joint research in this field of the physicist, biologist, and the clinic, will surely be fruitful of far-reaching results in the therapy of malignant tumors.

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